

WHAT IS CLAIMED IS:

1. A process for preparing simvastatin with a specified simvastatin dimer content, comprising the steps of:
 - a) lactonizing an ammonium salt of simvastatin in aromatic hydrocarbon at a concentration from about 25 to about 40 g/l to form a simvastatin;
 - b) dissolving the simvastatin in at least one solvent selected from the group consisting of toluene, ethylacetate, tetrahydrofuran, and benzene and precipitating the dissolved simvastatin with an anti-solvent selected from the group consisting of pentane, hexane, heptane, cyclohexane and petroleum ether; and
 - c) isolating the crystallized simvastatin,
wherein the crystallized simvastatin contains a simvastatin dimer content of about 0.2 to about 0.4% wt.
2. The process of claim 1, wherein the concentration of the ammonium salt of simvastatin is from about 30 to about 35 g/l.
3. The process of claim 2, wherein the concentration of the ammonium salt of simvastatin is about 35 g/l.
4. The process of claim 1, wherein the lactonizing step is performed by refluxing the ammonium salt of simvastatin in the aromatic hydrocarbon.
5. The process of claim 4, wherein the aromatic hydrocarbon is selected from the group consisting of benzene, ethylbenzene, xylene and toluene.
6. The process of claim 4, wherein the aromatic hydrocarbon is toluene.
7. The process of claim 4, wherein the lactonizing step is performed for about 3 to about 5 hours.
8. The process of claim 7, wherein the lactonizing step is performed for 4 hours.
9. The process of claim 1, wherein the lactonizing step is performed in the presence of butyl hydroxytoluene.
10. The process of claim 1, after step a) and before step b), further comprising the step of drying the simvastatin obtained in step a).
11. The process of claim 10, wherein the drying step is performed by evaporation.
12. The process of claim 10, wherein the simvastatin obtained in step a) is dried to residue by drying.
13. The process of claim 1, wherein the dissolving step is performed at about 60°C.
14. The process of claim 1, after step c), further comprises the steps of:

a) dissolving the simvastatin obtained in step c) in a water miscible organic solvent selected from the group consisting of methanol, ethanol, acetone, acetonitrile and tetrahydrofuran; and

b) adding an anti-solvent to induce precipitation to obtain recrystallized simvastatin.

15. The process of claim 14, wherein the water miscible organic solvent is methanol.

16. The process of claim 14, wherein the anti-solvent is water.

17. The process of claim 14, wherein the steps of d-e) are repeated.

18. The process of claim 1, wherein the crystallized simvastatin contains a simvastatin dimer content of about 0.25 to about 0.34% wt.

19. A process for preparing simvastatin with a specified simvastatin dimer content,

comprising the steps of:

a) lactonizing an ammonium salt of simvastatin in toluene at a concentration from about 25 to about 40 g/l to form a simvastatin;

b) dissolving the simvastatin in toluene and precipitating the dissolved simvastatin with hexane; and

c) isolating the crystallized simvastatin,

wherein the crystallized simvastatin contains a simvastatin dimer content of about 0.2 to about 0.4% wt.

20. The process of claim 19, after step c), further comprises the steps of:

d) dissolving the simvastatin obtained in step c) in methanol; and

e) adding water to induce precipitation to obtain recrystallized simvastatin.

21. The process of claim 20, wherein the steps of d-e) are repeated.

22. A process for preparing simvastatin with a specified simvastatin dimer content,

comprising the steps of:

a) lactonizing an ammonium salt of simvastatin in aromatic hydrocarbon at a concentration of less than about 60 g/l to form a simvastatin;

b) dissolving the simvastatin in at least one solvent selected from the group consisting of toluene, ethylacetate, tetrahydrofuran, and benzene and precipitating the dissolved simvastatin with an anti-solvent selected from the group consisting of pentane, hexane, heptane, cyclohexane and petroleum ether;

c) isolating the crystallized simvastatin;

d) dissolving the crystallized simvastatin in at least one solvent selected from the group consisting of toluene, ethylacetate, tetrahydrofuran, and benzene and

precipitating the dissolved simvastatin with an anti-solvent selected from the group consisting of pentane, hexane, heptane, cyclohexane and petroleum ether; and

e) isolating the recrystallized simvastatin,
wherein the recrystallized simvastatin contains a simvastatin dimer content of less than 0.2 % wt.

23. The process of claim 22, wherein the steps d) and e) are repeated.

24. The process of claim 22, wherein the concentration of the ammonium salt of simvastatin is from about 30 to about 35 g/l.

25. The process of claim 24, wherein the concentration of the ammonium salt of simvastatin is about 35 g/l.

26. The process of claim 22, wherein the lactonizing step is performed by refluxing the ammonium salt of simvastatin in the aromatic hydrocarbon.

27. The process of claim 26, wherein the aromatic hydrocarbon is selected from the group consisting of benzene, ethylbenzene, xylene and toluene.

28. The process of claim 26, wherein the aromatic hydrocarbon is toluene.

29. The process of claim 26, wherein the lactonizing step is performed for about 3 to about 5 hours.

30. The process of claim 29, wherein the lactonizing step is performed for 4 hours.

31. The process of claim 22, wherein the lactonizing step is performed in the presence of butyl hydroxytoluene.

32. The process of claim 22, after step a) and before step b), further comprising the step of drying the simvastatin obtained in step a).

33. The process of claim 32, wherein the drying step is performed by evaporation.

34. The process of claim 32, wherein the simvastatin obtained in step a) is dried to residue by drying.

35. The process of claim 22, wherein the dissolving step in b) or d) is performed at about 60°C.

36. The process of claim 22, after step e), further comprises the steps of:

f) dissolving the simvastatin obtained in step e) in a water miscible organic solvent selected from the group consisting of methanol, ethanol, acetone, acetonitrile and tetrahydrofuran; and

g) adding an anti-solvent to induce precipitation to obtain recrystallized simvastatin.

37. The process of claim 36, wherein the steps f-g) are repeated.

38. The process of claim 36, wherein the water miscible organic solvent is methanol.
39. The process of claim 36, wherein the anti-solvent is water.
40. The process of claim 22, wherein the crystallized simvastatin contains a simvastatin dimer content of less than about 0.19% wt.
41. A process for preparing simvastatin with a specified simvastatin dimer content, comprising the steps of:
 - a) lactonizing an ammonium salt of simvastatin in toluene at a concentration of less than about 60 g/l to form a simvastatin;
 - b) dissolving the simvastatin in toluene and precipitating the dissolved simvastatin with hexane;
 - c) isolating the crystallized simvastatin;
 - d) dissolving the crystallized simvastatin in toluene and precipitating the dissolved simvastatin with hexane; and
 - e) isolating the recrystallized simvastatin, wherein the recrystallized simvastatin contains a simvastatin dimer content of less than 0.2 % wt.
42. The process of claim 41, wherein the steps d) and e) are repeated.
43. The process of claim 41, after step e) further comprises the steps of:
 - f) dissolving the simvastatin obtained in step e) in methanol; and
 - g) adding water to induce precipitation to obtain recrystallized simvastatin.
44. A process for preparing simvastatin as in claim 1, wherein the ammonium salt of simvastatin is at least about 100 grams.
45. A process for preparing simvastatin as in claim 22, wherein the ammonium salt of simvastatin is at least about 100 grams.